

**PALM INTRANET**Day : Wednesday
Date: 3/7/2007
Time: 15:09:15**Inventor Information for 08/711339**

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or Patent#


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Attorney Docket #

Bar Code #

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L8 ANSWER 32 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1999:227936 CAPLUS <<LOGINID::20070307>>
 DOCUMENT NUMBER: 130:282070
 TITLE: Preparation of N-[[1-(4-cyanobenzyl)-1H-imidazol-5-yl]methyl]piperidines and analogs as farnesyl protein transferase inhibitors
 INVENTOR(S): Anthony, Neville J.; Gomez, Robert P.; Wai, John S.; Embrey, Mark W.; Fisher, Thorsten E.
 PATENT ASSIGNEE(S): Merck and Co., Inc., USA
 SOURCE: U.S., 91 pp.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5891889	A	19990406	US 1997-831308	19970401
US 6248756	B1	20010619	US 1999-248883	19990211
PRIORITY APPLN. INFO.:			US 1996-14791P	P 19960403
			US 1997-831308	A3 19970401
OTHER SOURCE(S):	MARPAT 130:282070			
GI				

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention is directed to compds. which inhibit farnesyl-protein transferase (FPTase) and the farnesylation of the oncogene protein Ras. The invention is further directed to chemotherapeutic compns. containing the compds., and methods for inhibiting FPTase and Ras farnesylation using them. In particular, title compds. I and II and their pharmaceutically acceptable salts are claimed [wherein Ar = (un)substituted Ph; R1 = H, Me; Q1 = (un)substituted (CH2)0-4; X = bond, CH2, CO, (un)substituted NHCO, S, SO, or SO2; Y = H, (un)substituted alkyl, OH or derivs., SH or derivs., NH2 or derivs., etc.; X1 = bond, (un)substituted NHCO or NH, O, S, SO, SO2; A1,A2 = bond, CH:CH, CO, O, (alkyl)imino, etc.; Q2 = (un)substituted (CH2)0-2; Z = (un)substituted aryl; addnl. substituents allowed on piperidine ring]. Over 130 invention compds. and numerous intermediates were prepared. For instance, the invention compound III was claimed in particular, and was prepared in 5 steps. Thus, Et isonipecotate underwent a sequence of: (1) N-protection with BOC; (2) deprotonation and alkylation in the 4-position using NaN(SiMe3)2 and 3-(CF3O)C6H4CH2Br; (3) reduction of the Et ester to a hydroxymethyl group using LiAlH4; (4) removal of the BOC group with HCl; and (5) reductive alkylation at N using 1-(4-cyanobenzyl)imidazole-5-carboxaldehyde and NaBH3CN, yielding III after chromatog. In a test for inhibition of farnesylation of Ras-CVIM with human FPTase in vitro, almost all example compds. had IC50 of $\leq 50 \mu\text{M}$.

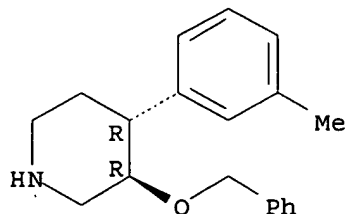
IT **198649-16-0P**
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of [[(cyanobenzyl)imidazolyl]methyl]piperidines and analogs as farnesyl protein transferase inhibitors)

RN 198649-16-0 CAPLUS

CN Piperidine, 4-(3-methylphenyl)-3-(phenylmethoxy)-, hydrochloride,
(3R,4R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



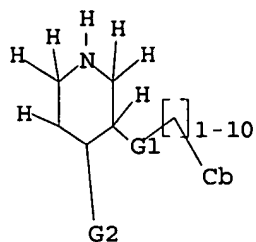
● HCl

REFERENCE COUNT:

21

THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d 11
 L1 HAS NO ANSWERS
 L1 STR



Cb ¹

2 O—Cb

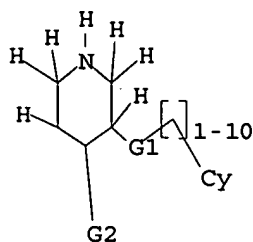
3 S—Cb

G1 O,S

G2 [@1], [@2], [@3]

Structure attributes must be viewed using STN Express query preparation.

=> d 19
 L9 HAS NO ANSWERS
 L9 STR



Cb¹

2 O—Cb

3 S—Cb

G1 O, S

G2 [01], [02], [03]

Structure attributes must be viewed using STN Express query preparation.

=> d his

(FILE 'CAPLUS' ENTERED AT 09:53:28 ON 07 MAR 2007)
DEL HIS

FILE 'REGISTRY' ENTERED AT 09:56:03 ON 07 MAR 2007

L1 STRUCTURE UPLOADED
L2 QUE L1
L3 3 S L1
L4 1234 S L1 FUL
L5 924 S L4 AND CAPLUS/LC
L6 310 S L4 NOT L5
L7 0 S L4 AND REF.CAPLUS>10

FILE 'CAPLUS' ENTERED AT 10:02:34 ON 07 MAR 2007

L8 36 S L4

FILE 'REGISTRY' ENTERED AT 10:12:48 ON 07 MAR 2007

L9 STRUCTURE UPLOADED
L10 QUE L9
L11 6 S L9
L12 1848 S L9 FUL
L13 614 S L12 NOT L4
L14 602 S L13 AND CAPLUS/LC
L15 12 S L13 NOT L14
L16 0 S L13 AND REF.CAPLUS>10

FILE 'CAPLUS' ENTERED AT 10:16:48 ON 07 MAR 2007
L17 18 S L13

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